3/9/2
DIALOG(R)File 351:Derwent WPI

016207258 **Image available**
WPI Acc No: 2004-365144/200434
Related WPI Acc No: 2004-365145
XRAM Acc No: C04-137879
Production of carbapenem derivatives for use as prodrug-type carbapenem preparations for oral administration in treating bacterial infection
Patent Assignee: MEIJI SEIKA KAISHA LTD (MEIJ)
Inventor: HORI N; OKUE M; YASUDA S
Number of Countries: 106 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200435539	A1	20040429	WO 2003JP13318	A	20031017	200434	B
AU 2003301425	A1	20040504	AU 2003301425	A	20031017	200467	

Priority Applications (No Type Date): JP 2002304630 A 20021018
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200435539	A1	J	54	C07D-205/08	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA
CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL
IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI
NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG
US UZ VC VN YU ZA ZM ZW
Designated States (Regional): AT BE BG CH CY CZ DE DK EA EE ES FI FR GB
GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ
UG ZM ZW

AU 2003301425	A1	C07D-205/08	Based on patent WO 200435539

Abstract (Basic): WO 200435539 A1

NOVELTY - A process for producing a compound of formula (IV) comprises the reaction between compounds of formulae (II) and (III).

DETAILED DESCRIPTION - A process for producing a compound of formula (IV) comprises the reaction between compounds of formulae (II)
and Mg(O2CCH2CO2R2) (III).

R1=hydroxyl-protecting group

R2=an in vivo degradable, easily removable group.

INDEPENDENT CLAIMS are also included for:

(1) compounds of formula (IV), (V), (VI), and (IX); and

(2) the use of compounds of formula (IV) as intermediate in the production of oral antibiotics.

R3=1-4C acyl, 1-4C alkylsulfonyl optionally 1-3 halogenated, 6-10C arylsulfonyl optionally 1-3 substituted with nitro, halo or 1-4C alkyl,

1-8C alkoxycarbonyl optionally substituted with 1-4C alkyl, 1-4C alkoxy, phenoxy, halo, nitro, phenyl, di-1-4C alkylamino, cyano, acetyl, benzoyl or di-1-4C alkylsulfamoyl, 6-10C aryloxycarbonyl optionally substituted with 1-4C alkyl, 1- 4C alkoxy, phenoxy, halo, nitro, phenyl, di-1-4C alkylamino, cyano, benzoyl or di-1-4C alkylsulfamoyl, or phosphoryl optionally substituted with 1-4C alkyl or phenyl.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - None given in source material.

USE - The produced carbapenem derivatives are for use as prodrug-type carbapenem preparations for oral administration in treating bacterial infection.

ADVANTAGE - Such compounds can be produced at lower cost on an industrial scale.

pp; 54 DwgNo 0/0

Technology Focus:

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Process: The reaction between compounds of formulae (II) and (III) is conducted in an organic solvent selected from tetrahydrofuran, acetonitrile, methylene chloride and ethyl acetate, in the presence of a base. Such base is particularly tri-1-4C alkylamine. The compound of formula (III) is obtained by reacting a malonic acid monoester of formula R2OCOCH2COOH (III') with a magnesium salt in an organic solvent. The process also includes a step of producing a compound of formula (II) by subjecting a compound of formula (I) or its salt to a reaction for imidazolide formation. During imidazolide formation, the compound (I) or its salt is allowed to react with N,N-carbodiimidazole, or with halogenated carboxylic ester and imidazole, in the presence of a base.

The compound thus produced is particularly of formula (XI).

R4=1-(1,4-thiazolin-2-yl)azetidin-3-yl or pyrrolidin-2-on-4-yl.

Such process also includes the reaction of compound (IV) with an azide compound to give a compound of formula (V), e.g. in an organic solvent chosen from tetrahydrofuran, acetonitrile, methylene chloride and ethyl acetate, in the presence of a base. The azide compound is particularly dodecylbenzenesulfonyl azide. After reacting the compound (V) with an acid, a compound of formula (VI) is obtained which is subjected to ring-closure reaction to form a compound of formula (VII), in a halogenated hydrocarbon solvent system in the presence of a metal catalyst like rhodium octanoate. Reaction of compound (VII) with an organic acid of formula (VIII), or a reactive derivative of phosphoric acid, affords a compound of formula (IX). R3OH (VIII) Such reactive

derivative is particularly diphenylchlorophosphate. The compound (IX) is reacted with a compound of formula HS-R4 (X) to form a compound of formula (XI).

Title Terms: PRODUCE; DERIVATIVE; PRODRUG; TYPE; PREPARATION; ORAL; ADMINISTER; TREAT; BACTERIA; INFECT

Derwent Class: B02

International Patent Class (Main): C07D-205/08

International Patent Class (Additional): C07D-477/04

File Segment: CPI

Manual Codes (CPI/A-N): B05-B01G; B06-D04; B07-D01; B14-A01

Chemical Fragment Codes (M2):

01 B614 B711 B720 B743 B831 F012 F013 F014 F015 F019 F140 F410 J0 J011 J012 J2 J271 J272 J5 J521 J522 J581 L472 L660 L9 L922 L941 M210 M211 M212 M213 M214 M215 M216 M220 M221 M222 M223 M224 M225 M226 M231 M232 M233 M240 M250 M262 M272 M281 M283 M311 M312 M313 M314 M315 M321 M322 M323 M331 M332 M333 M340 M342 M372 M373 M382 M383 M391 M392 M411 M510 M521 M522 M530 M540 M710 M720 M904 M905 N113 N211 N231 N315 P220 0130-59101-T 0130-59101-N 0130-59101-P

02 F012 F013 F014 F015 F019 F140 F410 H4 H401 H481 H8 J0 J011 J012 J2 J271 J272 J5 J521 J522 J581 K0 L472 L660 L7 L722 L9 L922 L941 M210 M211 M212 M213 M214 M215 M216 M220 M221 M222 M223 M224 M231 M232 M233 M240 M262 M272 M281 M311 M312 M313 M314 M315 M321 M322 M323 M331 M332 M333 M340 M342 M372 M373 M383 M391 M392 M413 M510 M521 M522 M530 M540 M710 M904 M905 0130-59102-N

03 B614 B711 B720 B743 B831 F012 F013 F014 F015 F019 F140 F410 J0 J011 J012 J2 J271 J272 J5 J521 J522 J581 K0 L472 L660 L7 L722 L9 L922 L941 M210 M211 M212 M213 M214 M215 M216 M220 M221 M222 M223 M224 M225 M226 M231 M232 M233 M240 M250 M262 M272 M281 M283 M311 M312 M313 M314 M315 M321 M322 M323 M331 M332 M333 M340 M342 M372 M373 M383 M391 M392 M411 M510 M521 M522 M530 M540 M710 M904 M905 0130-59103-N

04 B614 B711 B720 B743 B831 C316 D013 D014 D690 F012 F014 F015 F140 G001 G002 G010 G011 G012 G013 G020 G021 G022 G029 G040 G100 G111 G221 H103 H141 H181 H341 H381 H382 H383 H541 H581 H600 H608 H609 H641 H642 H643 H681 H682 H683 H684 H685 H686 H689 J0 J011 J012 J013 J2 J211 J221 J271 J5 J521 J522 J581 K353 K432 L143 L145 L472 L499 L640 L650 L660 L699 L9 L922 L941 M111 M112 M121 M122 M123 M125 M131 M137 M141 M150 M210 M211 M212 M213 M214 M215 M216 M220 M221 M222 M223 M224 M225 M226 M231 M232 M233 M240 M250 M262 M271 M272 M273 M281 M282 M283 M311 M312 M313 M314 M315 M316 M321 M322 M323 M331 M332 M333 M334 M340 M342 M343 M344 M349 M362 M373 M381 M383 M391 M392 M393 M411 M511 M520 M521 M530 M531 M532 M540 M710 M904 M905 0130-59104-N 41252

Ring Index Numbers: ; 41252

Generic Compound Numbers: 0130-59101-T; 0130-59101-N; 0130-59101-P; 0130-59102-N; 0130-59103-N; 0130-59104-N

Key Word Indexing Terms:

01 0130-59101-CL, NEW, PRD 0130-59102-CL, NEW 0130-59103-CL, NEW
0130-59104-CL, NEW

?